

4/15/13
96. (New) An FGM incorporating a substance to be preserved, formed according to the method of claim 94.--

Replacement pages for the claims (pages 31-40, 40a, and 40b) are provided herewith.

REMARKS

Applicants respectfully request reconsideration and allowance of the claims as amended in light of the remarks made herein.

Claims 1-77 are pending in this application, and stand variously rejected. By way of this amendment, the following claims are amended: Nos. 1, 6, 8-10, 12-23, 26-30, 36, 40, 42, 47, 49, 54-59, 61-67, 69-73, and 75. The following claims are canceled: Nos. 11, 24, 25, 43, 50, 51, 52, 53, 60, 68, 74, 76, and 77 without prejudice. New claims 78-96 are added. Support for the claim amendments and the new claims can be found throughout the specification and thus do not present new matter. Accordingly, all claims not canceled by way of this amendment are presently under examination.

The amendments have been made to advance prosecution of the present application, and are not intended to be a dedication to the public of any subject matter of the claims as originally presented.

Regarding Specification Amendments:

Entry of specification amendments is requested following Examiner's finding that certain recitations in claims 14-18, 26, 32, and 34 are not disclosed in the specification. An originally filed claim constitutes a description in the original disclosure in compliance with 35 USC § 112. See *In re Gardner* 177 USPQ 396, 397 (CCPA 1973). Accordingly, these amendments to the specification do not constitute entry of new matter.

Regarding Claim Amendments:

By way of this amendment, certain claims are amended and others are added to particularly point out and distinctly claim certain embodiments of the invention.

Claim 1 and certain other claims now recite exposing the syrup to reduced pressure at a temperature that causes boiling. Exposing the syrup to reduced pressure is described *inter alia* at page 18, lines 30-32 of the specification, and in the Examples. Claim 6 now recites certain carbohydrates listed in the paragraphs beginning on page 8, line 18 and page 8, line 32 of the specification. Claims 14 now recites conducting evaporation at a temperature higher than 25°C. Conducting evaporation above 25°C is supported *inter alia* on page 25, lines 18-21. Claim 36 recites adding an additive to the mixture prior to step (c). Page 12, lines 33-34 and Example 4a (page 26) describe adding various substances before the foaming step.

Claim 40 now recites a salt that decomposes under reduced pressure to give a gaseous product. This is supported *inter alia* on page 11, lines 5-6. Claim 47 recites a surface-active amphipathic molecule. This is supported *inter alia* on page 11, lines 29-30. Claim 54 now recites substances incorporated into FGMs which are cells, subcellular components, bacteria and viruses. This is supported *inter alia* on page 14, lines 4-5. Claim 56 now also recites peptides, hormones, and growth factors. Peptides are referred to on page 14, lines 16-17. Numerous hormones are listed on page 14, lines 17-32. Growth factors are referred to on page 14, line 19.

Claims 59, 69, 70, 73, and 75 refer to reconstitution by contacting FGMs with a solvent for the glass matrix forming material. Details of reconstitution are described on page 21, lines 7-21 and in the Examples. Other claim amendments are supported variously in the specification and in the claims as originally filed.

New claims 78 and 83 recite reducing residual moisture from the FGM. This is supported *inter alia* in claim 1 as originally filed. New claim 79 recites a syrup viscosity of 10^6 Pascal seconds. This is supported on page 17, lines 9-11. New claim 80 recites certain

preferred carbohydrates for formation of FGMs. These are supported on page 8, line 32 to page 9, line 2.

New claim 81 recites certain small molecules that may be incorporated in FGMs, which are listed on page 6, lines 13-17 and on page 13, lines 21-35. New claim 82 recites certain exemplary vaccine components. Hepatitis B surface antigen is described in Example 2b (page 23). Measles and polio virus are described in Example 5c (page 28 ff). New claims 86-89 recite various categories of substances incorporated into FGMs, supported on page 14, line 1 to page 15, line 32.

New claims 84 and 85 alternately describe substances in suspension or dissolved in the mixture used to form FGMs. This is supported *inter alia* on page 10, lines 18-21. Examples of molecular and macromolecular substances in suspension include Hepatitis B surface antigen (Example 5b, page 28) and measles and polio virus (Example 5c, pages 28-29). Examples of substances in solution include alkaline phosphatase and HSA (Example 5a, pages 27-28).

New claim 90 recites a residual moisture content of 0.1-5% (w/w), which is supported in the specification on page 20, lines 23-24. New claims 91-93 refer to producing FGMs using a volatile salt or a salt that decomposes at reduced pressure, as described on page 10, line 32 to page 11, line 14. New claims 94-96 refer to producing FGMs using a volatile organic solvent, as described on page 11, lines 15-25. Claims 92 and 95 further recite the exemplary carbohydrates trehalose, lactitol and palatinatate. This is supported on page 7, lines 28-31.

Accordingly, no new matter is added to the disclosure as a result of these amendments.

Informal Drawings:

In response to Examiner's finding that informal drawings filed with the application were not of sufficient quality to permit examination, applicants provide herewith a new set of photocopies of the same figures. Formal drawings will be provided upon allowance of the application.

Action on the Specification

The Examiner indicates that Table 1 is not found in the application. This is correct. By way of this amendment, reference to Table 1 on page 22 of the specification is removed. Table 1 is not required for the practice of this invention. Exemplary temperatures and drying times are provided in the other examples, and may be determined by routine observation.

The Examiner indicates that certain recitations in claims 14-18, 26, 32, and 34 are not disclosed in the specification. Reference to claim 31 was probably intended instead of claim 32. Support for the recitation of 30 mm Hg (claim 26) is found on page 18, line 31 of the specification. The recitations in claims 14-18, 31, and 34 are now also recited in the specification by way of the specification amendments herein.

Allowable subject matter

Applicants acknowledge with gratitude the Examiner's indication that the subject matter of claims 36-39, 48, 51, 56, and 58 are allowable if written in independent form. Related subject matter is recited in new claims 91-96. Applicants request immediate allowance of these claims.

Applicants maintain that the claims from which claims 36-39, 48, 51, 56, and 58 depend are also patentable, and thus have not rewritten these claims in independent form. Further support for this contention is presented in the sections that follow.

Claim rejections under 35 USC § 112 ¶ 1

Claims 1-77 are rejected under 35 USC § 112 ¶ 1, on the grounds that the disclosure is enabling only for claims using trehalose as the glass forming material. The Examiner correctly identifies trehalose as one of the preferred glass matrix forming materials. The Examiner then cites articles by Roser in BioPharm and New Scientist illustrating certain beneficial properties

of trehalose. The Examiner argues that since not all other glass matrix forming materials have these properties, the specification is non-enabling for generic claims.

This rejection is respectfully traversed. The rejection is effectively requiring all species in the generic claims to attain the features of a single specie. This is not the legal standard. The claimed invention is not limited to stabilizing labile proteins but, rather, to making foamed glass matrices and the products derived therefrom. Requiring the specification to support a limitation not found in the claims is not sufficient to uphold a 35 USC § 112, first paragraph rejection.

The references cited in the Office Action relate experiments in which the stability of the restriction enzyme *PstI* is tested after drying in various carbohydrate solutions. Experiments with enzymes such as *PstI* do not affect enablement of the claimed invention. The article in New Scientist describes restriction nucleases as “notoriously unstable enzymes”. In other words, *PstI* was chosen as an extreme example to test the properties of various sugars under the most rigorous conditions with respect to protein stabilization. The practitioner will readily appreciate that other sugars may be used with the present invention or even in the storage vehicles of the prior art. Other sugars can be used, for example, for the storage of substances not as sensitive to storage as *PstI*. Other sugars can also be used, for example, wherever the effects of reduction are not important.

In addition, the references cited in the Office Action make use only of the methods of the prior art. FGMs are not described. As related in the present disclosure, FGMs can be better depleted of residual moisture than prior art vehicles, and enhance the stability of substances stored in them. The relevance of the experiments in the cited art to storing even *PstI* to the claimed invention is entirely speculative.

Since the references are not clearly relevant to the claimed invention, and since the claimed invention is suitable for storage of a number of substances not tested in the references, the invention is not limited to trehalose as the glass matrix forming material. Accordingly, applicants are entitled to claim the glass matrix forming material generically. Although some experimentation may be necessary to determine the preferred sugar in a given situation, this

would be well within the skill of one in the art given the exhaustive experimental detail found in the specification. There is no evidence that one of skill in the art could not follow the instructions found in the specification to determine whether a particular glass matrix forming material is suitable for use. It is well settled that some experimentation does not constitute undue experimentation. Applicants request that this rejection be reconsidered and withdrawn.

A further rejection is made under 35 USC § 112 ¶ 1, on the grounds that the specification does not teach modifying the carbohydrate chemically or enzymatically. This presumably refers to claim 5. Claim 5 is also rejected under 35 USC § 112 ¶ 2. Not every experimental detail need be provided in a specification as one of skill in the art is presumed to know standard procedures. It is well within the skill of the ordinary artisan to modify carbohydrates using readily available materials and according to knowledge in the art. Also, many of these modified carbohydrates are commercially available. The ordinary artisan will readily appreciate that the list of exemplary carbohydrates on page 8 of the specification includes those obtained “by reduction” and by other chemical and enzymatic procedures, and that procedures not indicated or implied in the disclosure are nonetheless incorporated in the scope of the invention.

Claim rejections under 35 USC § 112 ¶¶ 2 and 4

Claims 1-77 are rejected under 35 USC § 112 ¶ 2 on the grounds that temperatures and pressures are not recited as “external”. By way of this amendment, claims 14-18 are amended to recite conducting the evaporation step at certain external temperatures. By way of this amendment, claims 19-23 are amended to recite conducting the evaporation step at certain external pressures. The use of the term “external” is otherwise unnecessary. Claims 1, 62, 65, 91, and 94 all incorporate a boiling step which involves *exposing* the syrup to a certain pressure and temperature. Claims not depending from these claims do not recite pressures or temperatures.

Claims 1, 62, and 65 are rejected under 35 USC § 112 ¶ 2 on the grounds that recitations of “evaporating bulk solvent” and “temperature sufficient to cause boiling” are vague and indefinite. By way of this amendment, these claims are amended to delete this language. Without agreeing with the Examiner’s position, applicants submit that the rejection is moot, and should be withdrawn.

Claim 5 is rejected under 35 USC § 112 ¶ 2 on the grounds that what is modified on the carbohydrate is not indicated. Claim 5 is discussed in the previous section, modifications to carbohydrates are within the skill of one in the art and need not be described in explicit detail.

Claims 6, 43, 55, and 58 are rejected under 35 USC § 112 ¶ 2 for allegedly improper Markush language. By way of this amendment, these claims are rewritten and now comply with 35 USC § 112 ¶ 2.

Claims 8, 59, and 61-70 are rejected under 35 USC § 112 ¶ 2 for reciting solvents without indicating what the solvent is dissolving. Applicants are grateful to the Examiner for the opportunity to clarify this matter. The solvents referred to in the formation and reconstitution of the FGMs are solvents for the glass matrix forming material. Unless otherwise required, additives and substances for preservation that are present in certain embodiments are not in solution, as both solutions and suspensions are acceptable (page 10, lines 18-21, and Examples 5a-5c). Amendments to these and other claims are provided herein to indicate in each instance the relationship between a solvent and its solute.

Claims 9 and 61 are rejected under 35 USC § 112 ¶ 2 on the grounds that recitation of a “biologically acceptable buffer” is vague and indefinite. By way of this amendment, these claims are amended to delete this language. Without agreeing with the Examiner’s position, applicants submit that the rejection is moot, and should be withdrawn.

Claim 14, 19, and 30 are rejected under 35 USC § 112 ¶ 2 on the grounds that recitation of “ambient temperature” is vague and indefinite. Claim 19 actually recites ambient pressure. Applicants maintain that these terms are understood by the ordinary artisan to refer to room temperature and atmospheric pressure. By way of this amendment, these claims are amended

to delete this language. Without agreeing with the Examiner's position, applicants submit that the rejection is moot, and should be withdrawn.

Claim 18 is rejected under 35 USC § 112 ¶ 2 on the grounds that recitation of "conditions sufficient to remove" is vague and indefinite. By way of this amendment, this claim is amended to delete this language. Without agreeing with the Examiner's position, applicants submit that the rejection is moot, and should be withdrawn.

Claim 47 is rejected under 35 USC § 112 ¶ 2 on the grounds that recitation of "amphipathic molecule" is vague and indefinite. Applicants traverse this rejection. Amphipathic is a well-defined term of art, referring to compounds that contain both strongly nonpolar and strongly polar groups. See, for example, Lehninger's "Biochemistry", 2nd edition, at page 43. The claim is amended to recite a "surface active" amphipathic molecule. No further limitation on the amphipathic molecule is intended.

Claims 50, 52, 53, 60, and 68 are rejected under 35 USC § 112 ¶ 2 on the grounds that various recitations are vague and indefinite. By way of this amendment, these claims are canceled without prejudice. Without agreeing with the Examiner's position, applicants submit that the rejection is moot, and should be withdrawn.

Claim 68 is rejected under 35 USC § 112 ¶ 2 on the grounds that the abbreviation "FRG" should be spelled out. The abbreviation was present in claim 69 as originally filed, and has been deleted by way of this amendment.

Claims 73-77 are rejected under 35 USC § 112 ¶ 2 as being vague and indefinite with respect to the recitation of "obtainable". By way of this amendment, claims 74, 76, and 77 are canceled, and the term *obtainable* is used in claims 71-73 and 75. The Examiner questions whether the compositions can be obtained. The rejection is improper, since the Examiner must indicate a reason for doubt, and fails to do so. For example, claim 1 recites a method for producing FGMs. The Examiner provides no showing that claim 1 is inoperable — to the contrary, illustrative examples are provided in Example 2-5 of the specification. Accordingly, FGMs are obtainable by the method of claim 1, and original claim 76 (amended claim 71) is neither vague nor indefinite. Similarly, claim 73 as amended herein recites a reconstituted

composition obtainable by preparing an FGM according to claim 62 and then contacting it with a solvent. The operability of claim 62 is illustrated in the Examples, and reconstitution by adding solvent is taught in the specification on page 21, line 7 ff. Applicants request that this rejection be withdrawn.

Claims 24 and 25 are rejected under 35 USC § 112 ¶ 4 for failing to further limit the subject matter of a previous claim. By way of this amendment, these claims are canceled. Without agreeing with the Examiner's position, applicants submit that the rejection is moot, and should be withdrawn.

Claim rejections under 35 USC § 102

Claims 1-4, 6, 8, 9, 13-18, 24, 30-36, 40, 41, 49, 52-55, 62, 63, 76 and 77, as originally filed, are rejected under 35 USC § 102(b) as being anticipated by Chivers (U.S. Patent No. 3,557,717). Claims 71 and 72 are rejected under 35 USC § 102(b) as being clearly anticipated by Wittlaufer et al. (U.S. Patent No. 5,290,765).

Applicants traverse both these rejections. For a rejection to be valid under § 102(b), a reference must teach within its four corners all the features of the method or composition which is claimed. Neither of the references cited attain this standard. Chivers and Wittlaufer et al. both teach noncrystalline amorphous solids or glasses; however, they do not teach the *structure* of the claimed products, or methods by which such structures can be obtained.

The claims under examination recite FGMs, methods of making FGMs, methods of reconstituting FGMs, and products obtained by reconstituting FGMs. The specification defines an FGM as a "high surface area *foamed* glass matrix"). An FGM is less dense than the solid amorphous glass, because of the increased surface area and the thinness of glass forming the *bubble walls* of the foamed glass matrix (page 7, lines 20-27; emphasis added). As recited in claim 1, FGMs are typically formed by obtaining a syrup, exposing the syrup to conditions that cause boiling or foaming, *and then allowing the composition to harden while still a foam*,

resulting in formation of the FGM. Formation of a hardened foam is further promoted by performing the boiling step at reduced pressure, which is now also recited in claim 1.

FGMs are novel over all prior art teachings of which applicants are aware, including the references cited in the Office Action under § 102. Chivers teaches an apparatus and process for making candy *floss*. Candy floss is defined in Chivers as candy in the form of fine fluffy *filaments* of sugar (column 1, lines 6-7). Chivers does not teach a hardened foam. The teachings of Wettlaufer et al. involve preparing solutions containing a vitrifying solute such as sucrose, and *drying* the mixture at approximately *normal atmospheric pressure* such that the vitrifying solute *achieves the vitrified state* (claim 1). Accordingly, an amorphous solid *film* forms in the bottom of the vessel used. There is no direction to induce foaming at any time in the process. Likewise, other forms of sample preservation known in the prior art, such as lyophilization, do not involve formation of a solid foam.

Since none of the references teach formation of a solid foam, and since the rejected claims involve formation of a solid foam, the rejection is invalid. Applicants respectfully request that this rejection be reconsidered and withdrawn.

Claim rejections under 35 USC § 103

Claims 10-12, 19-23, 25-29, 42-47, 50, 52-53, 57, 59-61, 64-70, and 73-75 are rejected under 35 USC § 103 as unpatentable over Chivers in view of Black (U.S. Patent No. 3,619,294), Samuels et al. (US Patent No. 5,422,384) and Wettlaufer et al. Claim 7 is rejected under 35 USC § 103 as unpatentable over Chivers in view of Roser (GB 2,206,273).

Applicants traverse both rejections. The rejections are insufficient to establish unpatentability for at least the following reasons: 1.) The references are from non-analogous arts, and cannot validly be combined under 35 USC § 103 with regards to the claimed invention; and 2.) Even when combined, the references do not teach or suggest FGMs. Elaboration of these reasons follows.

It is well established that teachings under disparate arts cannot be combined for purposes of a rejection under 35 USC § 103, absent of teaching or motivation to do so. The teaching or motivation must occur without the benefit of hindsight from the application under consideration.

An important case on the relevant art standard is *In re Clay* 23 USPQ2d 1058 (CAFC 1992), a copy of which accompanies this response. The following points are made:

- Whether arts are analogous requires determination of whether a reference is from the same field of endeavor, regardless of problem addressed; and if not, whether the reference is nonetheless reasonably pertinent to the particular problem with which the inventor is involved.
- Whether the field of endeavor is the same turns not on whether teachings are from the same industry, but the objective of the invention. Thus, inventions related to the *storage* of petroleum by Clay were from a different field of endeavor from inventions relating to *extraction* of petroleum taught previously.
- Whether a reference is reasonably pertinent to a particular problem turns on a similarity in *both* the structure and function. Clay's invention and the art cited against it both involved the use of a gel in processing petroleum. However, the gel of the cited art functioned to fill anomalies so as to improve flow properties, whereas Clay's gel functioned to displace liquid from the dead volume of a storage tank. The lack of functional similarity *alone* was sufficient to find that the reference was not reasonably pertinent under 35 USC § 103.

The claimed invention of the present application and the art cited in the Office Action are from a number of different fields of endeavor, and lack sufficient motivation to be combined.

The claimed invention relates to FGMs and methods of preparing them. As stated in the disclosure, FGMs are particularly useful for storing substances. As a storage vehicle, FGMs represent a substantial advance over those previously used for a number of reasons, including the ease of formation, stability imparted to the stored substance, the low moisture content

achievable, and the ease of reconstitution. With this function in mind, FGMs typically incorporate a complex bioactive substance or particulate, and are typically prepared in small aliquots.

Chivers teach apparatus and methods for the preparation of candy floss. This is clearly non-analogous art. Candy floss is designed not for long-term storage, but for immediate consumption. A filamentous structure is conferred on the hardened sugar, not to improve stability of a solute, but to improve its attractiveness. Dies are optionally added to floss, not for their preservation, but again to improve the appearance of the hardened sugar. The person of ordinary skill in the confectionery industry would not be motivated to add small molecule drugs, restriction nucleases, or viral particles to candy floss. Similarly, a person of ordinary skill in the pharmaceutical or biotechnology industry would not be motivated to look to the confectionery industry to solve the problems of drug storage. Accordingly, Chivers is non-analogous and irrelevant art in relation to the claimed invention. Chivers is also non-analogous to any of the other art cited in the Office Action, and cannot validly be combined with it.

Samuels et al. teach glass polymer composites and methods of making them. The list of organic and inorganic polymers for use with the Samuels invention listed in column 3, line 60 ff. are all covalent polymers. The working examples Samuels are all conducted with polybis(dimethylamino)-phosphazine, an inorganic covalent polymer. This is structurally different from typical embodiments of the present invention. The objective of Samuels et al. is to provide polymer/glass or polymer/ceramic composites with increased thermal stability, chemical stability, and enhanced fracture toughness, for use, for example, as fire retardants, optical windows, and protective coatings. The function, in other words, is to improve features of the glass or ceramic itself, not the preservation of something which may be dissolved or suspended within it. Accordingly, Samuels is non-analogous and irrelevant art in relation to the claimed invention. Samuels is also non-analogous to any of the other art cited in the Office Action, and cannot validly be combined with it.

Black et al. teach impregnated microcrystalline sugar granules. Since the granules are crystalline, they are structurally distinct from the present invention, and any of the other cited

art. The asserted utility of the Black invention relates to improving the taste, for example, of impregnated medicinals, providing sustained release, for example, of impregnated flavors, or preventing unwanted release, for example, of impregnated dyes (column 11, line 9 ff). The function is therefore distinct from the function of stabilizing storage and facilitating reconstitution of a solute or suspended particle. Accordingly, Black is non-analogous and irrelevant art in relation to the claimed invention. Black is also non-analogous to any of the other art cited in the Office Action, and cannot validly be combined with it.

The fact that these references are from non-analogous arts is sufficient to invalidate their use, either alone or in combination, as 35 USC § 103 references against the claimed invention.

Even if the references cited in the Office Action are combined, they do not teach or suggest the claimed invention.

Chivers teaches hardened sugar in a filamentous form. Either alone or in combination with the other references, Chivers does not teach or suggest FGMs.

Samuels et al. teach covalent polymers hardened into a glass or ceramic. Either alone or in combination with the other references, Samuels does not teach or suggest FGMs.

Black et al. teach impregnated microcrystalline sugar granules. Either alone or in combination with the other references, Black does not teach or suggest FGMs.

Wettlaufer et al. teach drying biological materials in the presence of vitrifying solutes under conditions that would result in formation of a vitrified film. Either alone or in combination with the other references, Wettlaufer does not teach or suggest FGMs.

Roser (GB 2,206,273) teaches impregnating foodstuffs with trehalose, and then drying the foodstuffs by heating. Either alone or in combination with the other references, Roser does not teach or suggest FGMs.

Claims under examination involve the formation of FGMs. Accordingly, the invention is patentable over the references cited in the Office Action. Applicants respectfully request that this rejection be reconsidered and withdrawn.

Patentability of New Claims

By way of this amendment, claims 78-96 are added. Claims 78-90 depend from claims already under examination, and include limitations thereof. Claims 91-96 relate to methods for producing FGMs involving use of a volatile salt, a salt that decomposes at reduced pressure, or a foam-promoting additive, and FGMs incorporating a substance to be preserved, formed according to these methods.

All of the newly added claims involve the formation of FGMs, and are patentable over the prior art of record for reasons already elaborated.

Conclusion

Following this amendment and the remarks made herein, applicants submit that the present application is in condition for allowance. Applicants respectfully request that all rejections be withdrawn and that all claims currently under consideration be allowed.

If a telephone interview would be of assistance in advancing prosecution of the present application, the Examiner is invited to telephone applicants' attorney at the number indicated below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952**. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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